ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 799

[OPPTS–42134E; FRL–4874–1]

RIn 2070–AC27

Proposed Revocation of Final Multi-substance Rule for the Testing of Neurotoxicity

AGENCY: Environmental Protection Agency (EPA).

ACTION: Proposed rule.

SUMMARY: The Environmental Protection Agency is proposing to revoke the Multi-Substance Rule for the Testing of Neurotoxicity at 40 CFR 799.5050, promulgated under section 4 of the Toxic Substances Control Act ("TSCA"), at 58 FR 40262, July 27, 1993. On October 8, 1993, the Chemical Manufacturers Association (CMA) and the manufacturers and processors of these substances filed suit seeking review of the rule in the 5th Circuit Court of Appeals. EPA is proposing to revoke this rule as part of a settlement agreement reached with the manufacturers of these chemicals, who have agreed to perform certain neurotoxicity and pharmacokinetics testing on 7 of the 10 chemicals subject to the final test rule, subject to execution of enforceable consent agreements ("ECA") containing these studies. Elsewhere in this **Federal Register**, EPA is announcing an administrative stay of the final rule pending final action on this proposed revocation.

DATES: Written comments on the proposed revocation of the test rule must be received on or before July 27, 1994.

ADDRESSES: Submit written comments identified by the document control number, OPPTS–42134E, in triplicate to: TSCA Public Docket Office (7407), Rm. NE B607, Office of Pollution Prevention and Toxics, Environmental Protection Agency, 401 M St., SW., Washington, DC 20460. A public version of the administrative record supporting this action, with any confidential business information deleted, is available for inspection at the above address from 12 noon to 4:00 p.m. Monday through Friday, except legal holidays.

FOR FURTHER INFORMATION CONTACT: Catherine Roman, Chemical Control Division, (7405), Office of Pollution Prevention and Toxics, 401 M St., SW., Washington, DC 20460, (202) 260–8155.

SUPPLEMENTARY INFORMATION: The Environmental Protection Agency is proposing to revoke the Multi-Substance Rule for the Testing of Neurotoxicity at 40 CFR 799.5050, promulgated under section 4 of the Toxic Substances Control Act ("TSCA"), at 58 FR 40262, July 27, 1993. On October 8, 1993, the Chemical Manufacturers Association (CMA) and the manufacturers and processors of these substances filed suit seeking review of the rule in the 5th Circuit Court of Appeals. The manufacturers of 7 of the 10 chemicals subject to the final test rule have agreed, subject to certain conditions set forth in the settlement agreement (Ref. 3), to conduct a set of neurotoxicity and pharmacokinetics testing under enforceable consent agreements ("ECA"). If ECA negotiations are successful, EPA believes that the previously issued final test rule would no longer be needed. EPA believes that, under a negotiated ECA, neurotoxicity and pharmacokinetics testing would be conducted and results made publicly available more quickly, and EPA resources used more effectively, than if EPA continued to litigate the merits of the final test rule.

The final test rule was published on July 27, 1993 (58 FR 40262), and requires manufacturers and processors of 10 substances to conduct testing for neurotoxicity. It is anticipated that the following seven substances would be tested pursuant to ECAs: acetone (CAS No. 67–64–1), technical grade *n*-amyl acetate (CAS No. 628–63–7), *n*-butyl acetate (CAS No. 123–86–4), ethyl acetate (CAS No. 141–78–6), isobutyl alcohol (CAS No. 78–83–1), methyl isobutyl ketone (CAS No. 108–10–1), and tetrahydrofuran (CAS No. 109–99–9). Testing is currently underway for *n*-butyl acetate and isobutyl alcohol. Pharmacokinetics testing would be conducted on butyl acetate to determine if its test results for neurotoxicity can be used to assess the neurotoxicity of its metabolite, 1-butanol. EPA does not anticipate entering into an ECA for 1-butanol (CAS No. 71–36–3), diethyl ether (CAS No. 60–29–7), or 2-ethoxyethanol (CAS No. 110–80–5), three other substances for which testing is required under the final test rule.

Elsewhere in this **Federal Register**, EPA is soliciting interested parties for participation in or monitoring of ECA negotiations. The settlement agreement signed by EPA and the parties to the lawsuit in April 1994 will be the starting point for the ECA negotiations.

I. Background

On July 27, 1993 (58 FR 40262) EPA issued a test rule under TSCA section 4 that required manufacturers and processors of ten substances to conduct testing for neurotoxicity (Ref. 1). The required testing was the same for all 10 substances and included acute and subchronic functional observational battery and motor activity, and subchronic neuropathology and schedule-controlled operant behavior. These 10 substances are listed below:

Chemical name	CAS No.
acetone	67–64–1
n-amyl acetate, technical grade	628–63–7
1-butanol	71–36–3
n-butyl acetate	123–86–4
diethyl ether	60–29–7
2-ethoxyethanol	110–80–5
ethyl acetate	141–78–6
isobutyl alcohol	78–83–1
methyl isobutyl ketone	108–10–1
tetrahydrofuran	109–99–9

The manufacturers of these substances petitioned for review of the final rule under TSCA section 19 in the Fifth Circuit Court of Appeals (Ref. 2). Subsequent to the filing of this challenge to the rule, EPA, the Chemical Manufacturers Association ("CMA"), and authorized representatives of all parties challenging the rule, entered into settlement negotiations to resolve the lawsuit.

As a result of these settlement discussions, CMA and the other parties to the lawsuit have agreed, subject to certain conditions set forth in the settlement agreement (Ref. 3), to conduct neurotoxicity and pharmacokinetics testing of seven chemical substances under negotiated ECAs, to be implemented by an order issued by EPA under TSCA section 4. Testing on two of the chemicals subject to the final rule, *n*-butyl acetate and isobutyl alcohol, is already underway. It is CMA's stated intent that such testing continue on schedule during the pendency of this proceeding (Ref. 3).

In turn, EPA has agreed to propose to withdraw the final test rule. EPA is aware that the settlement agreement contemplates a reduced set of testing on fewer chemicals than the testing regimen required by the final rule. Although EPA believes that the rulemaking record contains substantial evidence to support the testing requirements in the final rule, EPA has decided not to proceed with the litigation at this time. EPA believes that the uncertain outcome of the court's decision is outweighed by the benefits of allowing testing to proceed immediately. EPA believes that the settlement agreement is in the public interest as it will allow testing to proceed on an expedited basis, without the uncertainties of protracted litigation.

EPA notes that although CMA's lawsuit has been dismissed without prejudice by the 5th Circuit Court of Appeals, in response to a joint motion for a stay, it can be reinstated by either party upon filing of a letter with the court (Ref. 21). This Notice will allow all interested parties an opportunity to evaluate and comment on EPA's proposed revocation of the final rule and decision to pursue an ECA as the mechanism for achieving testing.

II. Testing Program

The testing program required for all 10 substances by the final test rule includes the following tests conducted according to the designated TSCA test guidelines:

Test	TSCA guideline
Functional observational battery, acute and subchronic	§798.6050
Motor activity, acute and subchronic	§798.6200
Neuropathology, subchronic	§798.6400
Schedule-controlled operant behavior (SCOB), subchronic	§798.6500

In the above tests, the test substance is to be administered to rats by the inhalation route of exposure in either a single exposure (acute) or repeated exposures over a 90–day period (subchronic). In both acute and subchronic studies, the test substance is to be administered to several groups of experimental animals, one exposure concentration being used per group. The animals are then to be observed under carefully standardized conditions with sufficient frequency to ensure the detection of behavioral and/or neurologic abnormalities over the range of exposures and also to determine the exposure level which results in no neurotoxic effect, i.e. no observed adverse effect level (NOAEL). The non-invasive functional observational battery is designed to detect gross functional deficits in young adult animals resulting from exposure to the administered chemical. The non-invasive motor activity test is designed to examine changes in the level and pattern of the animals' physical movement. These deficits and changes are also to be evaluated in the context of changes in other organ systems. The test for neuropathology is designed to detect and characterize morphologic changes in the tissue of the nervous system. The nervous system tissues are to be examined grossly and microscopically, beginning with tissues from animals in the highest dose group and proceeding to lower dose groups until a no observed adverse effect level (NOAEL) is determined. The non-invasive schedule-controlled operant behavior (SCOB) test is intended to evaluate the effects of repeated exposure to a chemical on performance of a learned behavior by measuring the rate and pattern of responding in relationship to the schedule of reinforcement.

In 1991 EPA updated its guidelines for neurotoxicity testing. The 1991 guidelines incorporate the functional observational battery, motor activity, and neuropathology into a single guideline entitled "Neurotoxicity Screening Battery." The SCOB test guideline remains a separate guideline. The 1991 guidelines evaluate the same endpoints as the older guidelines and also provide for greater flexibility in the conduct of the testing.

In September 1993, CMA requested, on behalf of its member companies subject to the testing requirements of the final rule, that EPA permit testing to be conducted according to the 1991 guidelines instead of the guidelines specified in the final test rule (Ref. 4). EPA agreed to this modification (Ref. 5). CMA also requested modifications of the test guidelines (Refs. 10, 14, 18 and 20) and modifications of the deadlines for submitting the test results (Refs. 10, 12, and 15). EPA granted most of these requests (Refs. 11, 13, 16, 17, and 19). The settlement agreement contemplates the retention of all modifications to the final rule's testing requirements in the anticipated ECAs.

The settlement agreement contemplates the execution of ECAs to conduct neurotoxicity and pharmacokinetics testing of the following 7 chemical substances:

Substance	Tests
acetone	SCOB (subchronic)
n-amyl acetate, technical grade.	Screening battery (acute and subchronic)
n-butyl acetate	Screening battery (acute and subchronic) SCOB (subchronic) Pharmacokinetics/metabolism
ethyl acetate	Screening battery (acute and subchronic) SCOB (subchronic)
isobutyl alcohol	Screening battery (acute and subchronic) SCOB (subchronic)
methyl isobutyl ketone.	SCOB (subchronic)
tetrahydrofuran	Screening battery (acute and subchronic)

Compared with the final rule, the above testing program represents a retention of the full set of tests for three chemicals (*n*-butyl acetate, ethyl acetate, and isobutyl acetate), a reduction in tests for four chemicals (acetone, *n*-amyl acetate, methyl isobutyl ketone, and tetrahydrofuran), and an elimination of testing for three chemicals (1-butanol, diethyl ether, and 2-ethoxyethanol). It is anticipated, however, that the pharmacokinetics/metabolism test of *n*-butyl acetate may indicate that the separate testing of 1-butanol may not be necessary, and because of this 1-butanol manufacturers have agreed to share in the cost of *n*-butyl acetate testing. The evaluation of the pharmacokinetics and metabolic fate of butyl acetate will be performed in a study of its in vivo hydrolysis to 1-butanol. If the conversion of butyl acetate to 1-butanol is sufficiently rapid and complete, EPA may determine that the neurotoxic effects of 1-butanol can be predicted from the results of butyl acetate testing. If this is not the case, EPA may consider reproposing separate testing of 1-butanol.

The anticipated testing programs for acetone and methyl isobutyl ketone (MIBK) include only the SCOB; the neurotoxicity screening battery for these two substances would be eliminated. EPA agreed to this change for the following reasons: The body of available toxicity data on both chemicals is considerable, and the available studies, which might, at some level, have shown the types of functional and morphologic effects which would be detected by the screening battery, do not indicate such effects. Furthermore, the SCOB test, as a test of performance dependent on learning and memory, evaluates a very different endpoint than those evaluated by the available toxicity studies. The SCOB may detect effects not seen in existing studies and represents a greater data gap for these chemicals. In the case of acetone, there is an additional reason for retaining the subchronic SCOB in the testing program. The acute SCOB test of acetone by Glowa and Dews was positive (Ref. 6), and EPA believes this positive finding bears further investigation in a repeated-dose test. For these reasons, EPA believes that this testing would represent a reasonable compromise which could avoid protracted litigation while still developing relevant data necessary to determine the neurotoxicity of these two chemical substances.

MIBK is currently listed as a hazardous air pollutant (HAP) under the Clean Air Act (CAA). EPA is considering initiating a TSCA section 4 testing program for several CAA HAPs, including MIBK. If neurotoxicity testing of MIBK is proposed under this HAPs testing effort, EPA believes that a delay of MIBK testing under the anticipated ECA would be warranted. The delay,

which would remain in effect pending the promulgation of the future HAPs test rule, would allow EPA and the MIBK test sponsors to coordinate testing efforts under the consent order and the future test rule to achieve the most efficient use of testing resources.

For both MIBK and acetone, EPA reserves the right to initiate future rulemaking or consent agreements if data from the SCOB tests, other section 4 test programs, or any additional new information indicate the need for such a step.

The anticipated testing programs for *n*-amyl acetate and tetrahydrofuran would include only the neurotoxicity screening battery; the SCOB tests would be eliminated. Given the limited nature of neurotoxicity testing on these chemicals, EPA believes that, at this time, the screening battery tests alone would represent an appropriate set of tests on these chemicals. Another factor influencing EPA's decision is that *n*-amyl acetate had the lowest production volume and lowest estimated exposure of all 10 substances in the final test rule. For these reasons, EPA believes that this testing would represent a reasonable compromise which could avoid protracted litigation while still developing relevant data necessary to determine the neurotoxicity of these two chemical substances. EPA, however, reserves the right to initiate future rulemaking or consent agreements if new information or the data developed from the screening battery tests of *n*-amyl acetate and tetrahydrofuran indicate a need for such a step.

The decision to propose to revoke all testing requirements for diethyl ether and 2-ethoxyethanol (2-EE) is primarily based on the estimated potential exposure to these substances. Diethyl ether has the second lowest production volume of the 10 substances in the test rule, which should directly influence potential exposure. A second consideration was that the available toxicity data on diethyl ether includes several human studies and more behavioral studies than were available on the other 9 substances.

In the case of 2-ethoxyethanol, EPA anticipates a reduction in the potential exposure estimated by the proposed and final rules. The environmental release of 2-ethoxyethanol has been confirmed to be on the decline by Toxic Release Inventory (TRI) data recently made available for the years 1990, 1991, and 1992 (Ref. 9). It is the only substance in the final test rule for which current information indicates that there is no consumer exposure, i.e. the producers of 2-EE who are parties to the settlement agreement have represented to EPA that there are no current consumer uses of the chemical (Ref. 3). To monitor the possible reemergence of any consumer uses of 2-ethoxyethanol, in the near future EPA intends to propose and promulgate a Significant New Use Rule ("SNUR") under TSCA section 5(a)(2) to require notification to EPA 90 days prior to the manufacture, import, or processing of 2-EE for use in a consumer product. The parties to the agreement have agreed not to oppose such a rule (Ref. 3). Concerning occupational exposure to 2-ethoxyethanol, EPA believes that if the recently proposed OSHA health standard for 2-ethoxyethanol (58 FR 15526, March 23, 1993) becomes effective it should reduce the likelihood of occupational exposure (Ref. 7). OSHA's regulatory agenda schedules this health standard to be finalized as soon as April 1995 (Ref. 8). Should the implementation of the OSHA health standard be significantly delayed because of a legal challenge or if the consumer use of 2-ethoxyethanol reemerges, EPA may feel compelled to reconsider proposing testing at that time. As stated earlier, EPA reserves the right to initiate future rulemaking or consent agreements on these two substances if it appears warranted at that time.

III. Proposed Revocation of Final Test Rule and Issues for Comment

Based upon the reasons stated above, EPA is proposing to revoke the final Multi-Substance Rule for the Testing of Neurotoxicity (40 CFR 799.5050). The decision to allow manufacturers of these substances to conduct neurotoxicity and pharmacokinetics testing under ECAs should allow for the most timely development and public availability of data to assess the potential neurotoxicity of these compounds. While EPA acknowledges that the testing that may be conducted under ECAs may not be as extensive as that required by the final test rule, EPA believes that use of the ECA process will result in the fastest development of data. Testing and data development will proceed without the potentially lengthy delay of testing pending resolution of costly litigation on the merits of the final test rule.

IV. Rulemaking Record

EPA has established a record for this proposed revocation under docket no. OPPTS–42134E. This record contains the information EPA considered in reaching the settlement agreement and the following information:

A. Supporting Documentation

(1) **Federal Register** notices pertaining to this proposed rule consisting of:

(a) Notice of proposed multi-substance rule for the testing of neurotoxicity (56 FR 9105, March 4, 1991).

(b) Notice of final multi-substance rule for the testing of neurotoxicity (58 FR 40262, July 27, 1994).

(2) Communications consisting of:

(a) Written letters.

(b) Contact reports of telephone conversations.

(c) Meeting summaries.

B. References

(1) Final multi-substance rule for the testing of neurotoxicity (58 FR 40262, July 27, 1993).

(2) Chemical Manufacturers Association (CMA). Petition for Review. Filed with United States Court of Appeals for the Fifth Circuit. (October 8, 1993).

(3) United States Court of Appeals for the Fifth Circuit. Settlement Agreement between Environmental Protection Agency (USEPA) and petitioners. No. 93–5381. (April 28, 1994).

(4) CMA. Letter from Gordon Strickland to Michael Stahl, Office of Compliance Monitoring, Office of Pollution Prevention and Toxics (OPPT), USEPA, Washington, DC. (September 16, 1993).

(5) USEPA. Letter from Charles Auer, Chemical Control Division (CCD), OPPT to Gordon Strickland, CMA, Washington, DC. (September 21, 1993).

(6) Glowa, J.R. and Dews, P.B. "Behavioral toxicology of volatile organic solvents. IV. Comparisons of the rate-decreasing effects of acetone, ethylacetate, methyl ethyl ketone, toluene, and carbon disulfide on schedule-controlled behavior of mice." *Journal of the American College of Toxicology*. 6:461–469. (1987).

(7) Occupational Safety and Health Administration (OSHA). Proposed rule: "Occupational exposure to 2-methoxyethanol, 2-ethoxyethanol and their acetates (Glycol ethers)." 58 FR 15526 (March 23, 1993).

(8) OSHA. Regulatory Agenda. "Glycol ethers: 2-methoxyethanol, 2-ethoxyethanol, and their acetates." 59 FR 20647. (April 25, 1994).

(9) USEPA. Toxic Release Inventory (TRI). Total annual environmental releases of 2-ethoxyethanol for the years 1987 through 1992. TRI printouts. (May 6, 1994).

(10) CMA. Letter from Barbara Francis to Charles Auer, CCD, OPPT, USEPA. (September 30, 1993).

(11) USEPA. Letter from Charles Auer, CCD, OPPT to Barbara Francis, CMA. (October 18, 1993).

(12) CMA. Letter from Gordon Strickland to Michael Stahl, OCM, OPPT, USEPA. (October 26, 1993).

(13) USEPA. Letter from Charles Auer, CCD, OPPT to Gordon Strickland, CMA. (November 4, 1993).

(14) CMA. Letter from Barbara Francis to Charles Auer, CCD, OPPT, USEPA. (November 5, 1993).

(15) Latham Watkins, Counselors for CMA. Application for Stay or modification of acetone testing. (November 5, 1993).

(16) USEPA. Letter from Charles Auer, CCD, OPPT to Barbara Francis, CMA. (November 9, 1993).

(17) USEPA. Letter from Charles Auer, CCD, OPPT to William Rawson, CMA. (November 17, 1993).

(18) CMA. Letter from Barbara Francis to Charles Auer, CCD, OPPT, USEPA. (March 17, 1994).

(19) USEPA. Letter from Charles Auer, CCD, OPPT to Barbara Francis, CMA. (April 12, 1994).

(20) CMA. Letter from Barbara Francis, CMA, to Charles Auer, CCD, OPPT, USEPA. (June 17, 1994).

(21) United States Court of Appeals for the Fifth Circuit. Dismissal of petitioners appeal against EPA. No. 93–5381. (May 13, 1994).

The public record for this rulemaking is available for inspection in the TSCA Nonconfidential Information Center (also known as the TSCA Public Docket Office), Rm. NE B607, 401 M St., SW., Washington, DC from 12 noon to 4:00 p.m., Monday through Friday, except legal holidays.

V. Regulatory Assessment Requirements

A. Executive Order 12866

Under Executive Order 12866 (58 FR 51735, October 4, 1993), the Agency must determine whether the regulatory action is "significant" and therefore subject to all the requirements of the Executive Order (i.e., Regulatory Impact Analysis and review by the Office of Management and Budget (OMB)). Under section 3(f), the order defines "significant" as those actions likely to lead to a rule (1) having an annual effect on the economy of $100 million or more, or adversely and materially affecting a sector of the economy, productivity, competition, jobs, the environment, public health or safety, or State, local, or tribal governments or communities (also known as "economically significant"); (2) creating serious inconsistency or otherwise interfering with an action taken or planned by another agency; (3) materially altering the budgetary impacts of entitlements, grants, user fees, or loan programs; or (4) raising novel legal or policy issues arising out of legal mandates, the President's priorities, or the principles set forth in this Executive Order. Pursuant to the terms of this order, EPA has determined that this rule would not be "significant."

B. Regulatory Flexibility Act

Under the Regulatory Flexibility Act, 5 U.S.C. 601 et seq., EPA is certifying that revocation of this test rule would not have a significant impact on a substantial number of small businesses because only the 28 manufacturers who sign the anticipated ECAs will be responsible for conducting and paying for the testing. None of these manufacturers are small businesses.

C. Paperwork Reduction Act

There are no information collection requirements associated with this proposed revocation covered under the provisions of the Paperwork Reduction Act of 1980, 44 U.S.C. 3501 et seq.

List of Subjects in 40 CFR Part 799

Chemicals, Chemical export, Environmental protection, Hazardous substances, Health effects, Laboratories, Reporting and recordkeeping requirements, Testing.

Dated: June 18, 1994.

Lynn R. Goldman,

Assistant Administrator for Prevention, Pesticides and Toxic Substances.

Therefore, 40 CFR, chapter I, subchapter R, part 799 is proposed to be amended as follows:

PART 799—[AMENDED]

1. The authority citation for part 799 would continue to read as follows:

Authority: 15 U.S.C. 2603, 2611, 2625.

§799.5050 [Removed]

2. By removing §799.5050.

[FR Doc. 94–15567 Filed 6–24–94; 8:45 am]
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